A PARTIAL STUDY OF ULCERATIVE ENDOCARDITIS.

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The subject of ulcerative endocarditis formed the thesis of Dr. Osler's Goulstonian Lectures in 1885. He begins them as follows:

"It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future."[1]

It is with this spirit I have undertaken a renewed study of ulcerative endocarditis.

In 1898 Sir Douglas Powell delivered before the Royal College of Physicians of London "Lectures on the Principles which Govern Treatment in Diseases and Disorders of the Heart."[2]

In this third lecture he carefully considered those which specially dominate the treatment of ulcerative endocarditis. There he also reviewed the therapeutic measures likely to be of some use in the disease. He likewise gave a tabulated statement of the results of treatment by antistreptococcic serum, and of his own experience with yeast and with nuclein, after the method of Dr. V. C. Vaughn, of Michigan. In the Lumleian Lectures during the current year, Dr. T. R. Glynn[3] has again reviewed this subject and regarded it "mainly in its clinical aspects." He was influenced to do so because of its great clinical interest, and the fact that no disease presents itself under a greater variety and perplexity of forms. A very elaborate historic retrospect of our growing knowledge pertaining to the disease is at first dwelt upon. In it he cites Matthew Bailey, Morgagni, Senac, Corvisart, and Bouillaud. To the latter he ascribes the honor of associating ulceration of the cardiac valves with symptoms of typhoid fever. He shows how the "third period" was marked by a perfected bacteriological technique, and by the fuller comprehension of the biological characteristics of bacteria. Thus ulcerative endocarditis, which was formerly considered as a local affection, is now regarded as one of the complications of a general infection.

This malady, like the simple form of endocarditis, affects the lining membrane of the heart and especially the nerves. It is characterized by vegetations and is accompanied with loss of tissue. The ulceration may cause perforation of heart valves, or even of the septum or heart walls, under very exceptional conditions. With the ulceration we may find a limited area of suppuration. It is very rarely a primary affection, but ordinarily occurs as a complication of some infective disorder, or septic disease. No doubt this view explains how it is that the lesions of simple endocarditis often precede and are found in conjunction with those of the more advanced or far graver form of the disease. Between the latter and the benign malady there is, indeed, no essential anatomical difference, and they merely represent gradations, as it were, of more or less intensity.

Although cases which have developed primarily are occasionally observed, they are so infrequent as to have had legitimate doubt thrown on them. Osler reports one case in which at the autopsy no lesions were found other than those of ulcerative endocarditis.[4] In cases of obscure origin it is probable that the micro-organisms frequently enter the economy by the respiratory passages, and reach the heart in this way rather than through the digestive organs. Especially in cases of chronic heart trouble by reason of secondary congestion of the air-passages, the conditions become favorable to bacterial invasion. An infective endocarditis originating in this way would occasionally appear to be of primary origin. (Glynn.)

On the other hand, ulcerative endocarditis occurs quite frequently as a complication of pneumonia. "In 16 cases of 100 autopsies in which this lesion was present, 11 were of this form."[5] According to Wells, the proportion in all cases of pneumonia is 3 per cent., while the percentage in fatal cases of the latter disease is 4 per cent. G. Studa's estimate of the relative frequency of ulcerative endocarditis in pneumonia is a much higher one (9 cases in 85 autopsies).[6] When it is found in this disease it appears to be exceptionally virulent, as numerous autopsies demonstrate. It is also seen in acute rheumatism. Anders[7] writes that the proportion is about 10 per cent. of the cases in which acute endocarditis appears. It may also occur as a complication of some eruptive fevers and in septicæmia. Vaccination has been followed by cellulitis and infective endocarditis. (Coleman.)

Cases are likewise due to dental caries and oral sepsis. When we consider the great number of cases of acute and subacute rheumatism we are called to treat, the number of those complicated with ulcerative endocarditis seems very small.

Ulcerative endocarditis often follows septicæmia of various origin, and is not uncommon in gonorrhœa. The intimate relations between some cases of gonorrhœa and ulcerative endocarditis have been established for more than twenty years, but it is only lately that these instances have been studied in a systematic manner.[8] A fatal case of this kind has been reported.[9] In some of these cases it has been impossible from the most careful local researches to discover the site of entrance of the infective disease. We should then turn to cultures made from the blood, and occasionally bacteria with the typical characteristics of gonococci will be shown.[10]

The cultivation should be made during life, and it may be confirmed at the autopsy from blood taken from the heart, or from the cardiac vegetations. For the cultivation it is not essential to take a great deal of blood, to dilute it much, or to make use of special media. It is now known, also, that the bactericidal action of the blood is less pronounced on gonococci than it is on pneumococci or the typhoid bacillus. The septic process that proceeds from the puerperal state is also a well-known source of grave ulcerative endocarditis. Although certain authors have described it as a complication of malaria, it is questionable whether such cases often occur. Among diseases which are occasionally complicated with malignant endocarditis I would cite measles, scarlatina, smallpox, erysipelas, and typhoid fever. In my experience such instances, with the exception of the latter disease, have not been seen, and even of this finding I have no available record.[11]

Cerebral complications are associated with it at times, particularly, as meningitis,[12] and this is especially true when the malignant endocarditis is found with pneumonia. I have observed one caseof obscure mental disorder in which the malignant endocarditis was shown to be "mural" at the autopsy, and no gross changes had taken place in the brain. Miliary abscesses have been found, however, in a number of instances. Once Jackson found an embolus of the artery of the Sylvian fossa, and Lartigau[13] reports a case of gonorrhœal origin, in which prior to death there was a sudden aphasic attack. The bacillus of influenza has also been detected in the valvular vegetations of ulcerative endocarditis. The cases observed were instances of the development of the disease upon a chronic cardiac affection.[14]

This fact is important as pointing to a demonstration of what has long been considered probable, namely, the vulnerability of the heart to the influenza poison. Ulcerative endocarditis occurred in 4 of de Batz's 20 cases, and a most interesting example has been recorded by Tickell. It has been observed during the influenzal attack, but most frequently in the convalescing period.[15]

A new organism of endocarditis, called micrococcus zymogenes, has lately been pointed out in a patient who died. The infarcts which accompanied this case are not stated to be other than bland; therefore it may be that the endocarditis itself belonged to the simple type. On the other hand, Maccullum and Hastings report a case caused by this organism, in which multiple septic infarctions in various viscera were found. Further, typical acute vegetative endocarditis was experimentally produced by intravenous inoculation in a rabbit and a dog, and the cocci were demonstrated in pure culture in the vegetations and in other parts of these animals after death. The micrococcus zymogenes is stated to be extremely minute, often elliptic in outline, usually found in pairs, is not motile, and stains with the ordinary stains.[16]

Although it is stated by some writers that the two forms of the disease, simple and ulcerative, never become one and the same, this affirmation is probably too positive. Litten believes that prompt response to the salicylates is characteristic of the benign form.[17] They may be used, therefore, with some measure of reliance to determine an otherwise doubtful diagnosis. Litten also criticises Lenhartz's views as to the fact that the finding of micro-organisms in the blood characterizes the endocarditis as septic. Very justly he remarks that if later the microbe of acute rheumatism be accurately determined, such distinction will be no basis to rest upon. In the septic-malignant form of Litten, suppuration occurs in thrombi and joints, which does not occur in the non-septic malignant form. He objects strongly to the term "ulcerative" endocarditis, but does not believe the time has come to make separations on the ground of the presence or differences of micro-organisms. Poynton and Paine consider that ulcerative and other forms are only different degrees of the same disease, and that benign forms may become malignant under the "influence of virulent breeds" of the common micro-organism of rheumatism. Ewart insists that, even though the practical identity of the organisms may not be proven, a very important clinical lesson is furnished. This essentially means that our efforts of prophylaxis in rheumatism should be strengthened, because in prophylaxis of this disease we also combat the development of most serious cardiac affections.[18] An equally important matter has already been insisted upon by Sir Douglas Powell in his Lumleian Lectures where he directs "attention to the necessity of observing certain prophylactic precautions during convalescence in rheumatic endocarditis" (*loc. cit.*, p. 1153). The lesions found may be in the heart, or other organs of the economy.

In Jackson's cases enlargement of the spleen was present in all but one instance. Leukocytosis was also regularly found, the leukocytes usually numbering from 16,000 to 20,000. This is an important point in the differential diagnosis from malaria, tuberculosis, and typhoid fever. The bacteria in the blood are important and have different forms. In 23 cases studied bacteriologically by Jackson "in 2 no cultures were obtained; in 2 there were micro-organisms which were not identified; in 8 streptococcus pyogenes was found; in 5, the pneumococcus; in 3, staphylococcus aureus; in 1, the colon bacillus; in 1, the streptococcus and staphylococcus; and in 1, the streptococcus with other organisms."

In the 38 cases discussed by Lenhartz, the author carried out bacteriological investigations in 28 cases. In 16 cases bacteria were found during life. They were principally staphylococci. According to Lenhartz it is usually comparatively easy to find the organism in the blood.[19] From the point of view of prognosis it is very desirable to differentiate between the various forms of ulcerative endocarditis. This may be accomplished by careful blood cultures during life. It is especially desirable at present, by reason of the more hopeful outlook of these cases. This seems to be proven partly by the results from treatment, partly by the data afforded by careful autopsies. Ewart, indeed, has stated, even in cases that resulted fatally, that evidences of repair in the local cardiac lesions could be shown. It may be remarked that there is little tendency in this process toward *cicatrization*, so that recovery may take place with little or no deformity of valves or orifices. (Wells.) The cardiac changes will depend upon the nature of the organisms which occasion them, and also upon the extent and duration of the disease. We do not find the same conditions in instances in which the process is wholly acute, and those where the acute disease is attached to former sclerotic changes of the valves. Usually we find vegetations on the valves. These are often found with an ulcerative process and small abscesses. According to Wells the distinguishing features of them are their massive character and broad base. Moreover, they do not extend often beyond the valves. The left heart is more frequently the site of the disease than the right. In regard to this point errors may be found in literature. Still the right heart is attacked oftener than in the benign form.

Mural ulcerative endocarditis is extremely rare. I have seen only one case, to which I have referred. The history of another one, hitherto unpublished, has been kindly given to me by my colleague, Dr. Van Horne Norrie. In rare instances the process may extend to the aorta and pulmonary artery. A secondary infective arteritis in various peripheral situations and in the different viscera, as a result of septic embolism from the heart, may also occur.[20] The vegetations are frequently small, especially when they alone are present. They are of gray or yellow color, and are situated on the margin or at the base of the valves. Under the microscope they are shown to be composed of numerous microbes, embryonic cells, and leukocytes. They also contain fibrin.[21] In many instances, however, the vegetations are larger and may become pedunculated. They have a markedly gray aspect also, or are covered with blood clot, and often show superficial or deep ulceration of tissue. In the latter case an aneurysmal pouch may be found. This pouch formation doubtless is due to blood pressure upon softened and degenerated valvular tissues. Sometimes the ulceration goes deep enough to make a perforation of the valve. Again, it extends to the chordæ tendineæ, beginning in the inflammatory stage, and separates later the valve segment completely. When this takes place we may have a flapping with each ventricular contraction of the detached valve against the auricle. Thus, secondary infection of the auricular walls is produced, and it is not uncommon to find warty growths here situated. In rare instances when the ulceration has enlarged and become still deeper, the septum or ventricular walls may be perforated. If the malignant endocarditis be caused by pyogenetic organisms it is not uncommon to find small abscesses in the valves, or, indeed, in other parts of the heart. These abscesses may rupture, sometimes with perforation of the heart walls, and then pus is found in the pericardial sac. It is also possible for small quantities of pus to be reabsorbed, and the evidence of this is found in old scar tissue, or calcareous deposits. In some cases, especially when malignant endocarditis is found in a patient suffering from chronic heart disease, the vegetations may be capped with calcareous incrustations. In very rare instances the deposit of lime salts may occur in acute cases.

The ulcerative condition of malignant endocarditis may possibly be confounded with that which follows the necrosis of former atheromatous deposits, or those incident to chronic rheumatic endocarditis of benign nature. A differential diagnosis may here be made, probably with the use of the microscope; but at times doubt may still remain. Osler, in an analysis of 209 cases, showed the proportion in which the different valves, the walls, and sides of the heart are involved. His report reads "aortic and mitral valves together, 41; aortic valves alone, 53; mitral valves alone, 77; tricuspid in 19; pulmonary valves in 15, and the heart wall in 33 instances. In 9 instances the right heart alone was involved; in most cases, the auriculoventricular valves."[22] In Strada's 85 autopsies the seat of the affection was in the left side of the heart alone in 6 cases, and in the right alone in 3 cases. In Jackson's 43 examinations post-mortem we find that "the aortic valves were affected in 9 instances; the mitral, in 15; both, in 10. The right side of the heart was involved 6 times, and the endocardium of the ventricle 3 times. In 5 of the aortic cases there was old endocarditis; it was present in 7 of the mitral cases. The malignant disease had become implanted upon the old disease."

The mechanical factor, however, is not considered essential by Lenhartz, and he has shown that fresh endocarditis does not always arise at the site of the old endocarditis if the latter is present. In Glynn's cases "the infective endocardial lesions were distributed as follows: the aortic and mitral valves were involved in 21 cases, the aortic in 10, the mitral in 15, and the endocardium of the ventricle alone in 1. The right side of the heart was involved in 6 instances" (*loc. cit.*, p. 1073.) Mural endocarditis is apt to affect either the upper portion of the septum of the left ventricle or the posterior wall of the left auricle.

According to the analysis of Kantback and Tickell, in 84 cases there were 51 males and 33 females; and in all but 16 cases old cardiac lesions were found. (Allbutt, p. 877.[23]) In Glynn's cases he found 65 per cent. of patients were males and 34 per cent. were females—"figures approximating those of Dr. Osler." The disease occurred, however, more frequently in young women than in young men. It was also remarked that the disease was likely to occur under conditions attended with general debility. In only

7 per cent. of the cases had an inflammation of the lungs preceded the endocarditis; in 11 per cent. of his cases the endocarditis originated in a recognized infective focus. The vegetations may become detached in larger or smaller masses and, carried by the circulation, form embolic plugs in different organs. Notably we find the kidneys and spleen affected; less frequently the brain and intestines are involved. The place where the embolic mass is arrested depends largely upon its size. While small emboli are more apt to be seen, it is not unknown to have a large artery completely obstructed. If the lungs contain infarcts, the embolic plugs originated in malignant endocarditis affecting the right heart. The embolic plugs are more or less numerous. In some cases where the malignant endocarditis is very pronounced and the ulcerative condition extensive, the autopsy does not show any embolic processes in the organs. They are also more or less irritating.

Consequent upon the degree of their infective nature follows the rapidity with which abscesses are formed. At the site of these abscesses it is not uncommon to find the arterial vessel already softened and ulcerated. Very many small abscesses are found at times in different organs of the body. Sometimes hemorrhage may be combined with the abscesses. Why in some cases the one is more frequent than the other is not positively known. (Strümpell, *Practice of Medicine*, 1901, p. 306.) Embolism was found to be "nearly three times as frequent in the infective as in the simple cases." (Glynn, p. 1076.) It is noted, contrary to the usually accepted opinion, that the so-called infarcts are not due to embolism, but are the result of "apoplexies" following the rupture of small bloodvessels, and made "specially liable to occur in severe passive congestion of the lungs."

. The micro-organisms found in malignant endocarditis are pneumococci, streptococci, staphylococcus pyogenes aureus and albus, the gonococcus, and other organisms. The former are most frequently concerned, either alone or associated with others. The pneumococcus infection is more frequent in aortic endocarditis, the streptococcus infection in mitral endocarditis.[24] While in septic diseases malignant endocarditis is prone to occur, there are cases in which the valves are but slightly involved. In no case does the endocarditis form more than a part of the general septic condition. If, however, the heart is notably affected, it hastens very much the spread of the poison, and thus this organ becomes very important in the estimate of the gravity of the case. Of course, there is in these cases the local disease of which the malignant endocarditis is the result. This may be of the nature of an acute necrosis, a wound abscess, or puerperal disease, when there may be primary septic foci in the uterus, or its adnexa.

The etiology of the disease is varied. This is known. Many cases follow an infectious disease, especially pneumonia. This fact has been pointed out by Osler. Still there are cases which appear to be primary (Jackson), as no assignable or sufficient cause of their development can be discovered. All forms of endocarditis, whether ulcerative or benign, seem, according to later investigations, to be of parasitic origin.* This view had been entertained also by Bartel. According to this author, in cases of rheumatic origin the organisms soon die, and often are not discoverable, particularly in cases which have run a somewhat chronic course. There are, however, some cases which "are apparently not due to the direct action of micro-organisms." These are caused by thrombotic deposits, and are possibly the results of the action of bacterial toxins.†

In a peculiar case of endocarditis reported by Hopkins and Weir, in which death resulted from cerebral hemorrhage, we have one that "seems to belong to the group on the border-land between a septic and ulcerative endocarditis; all the emboli were simple, not septic."‡

Thayer and Lazear[25] have gone thoroughly into the subject of gonorrhœa as a cause of septicæmia and ulcerative endocarditis. In their paper they show that the discovery of the gonococci in the circulating blood and upon the cardiac vegetations was made by Blum in 1895. The endocardium may be directly attacked by the gonococcus, as the general infection may be the immediate cause of the local trouble.

Ulcerative endocarditis is a rare disease in childhood. When it does occur in childhood it does not differ essentially from the disease in the adult. One case is reported in an infant ten months old, by L. D'Astros,[26] which resulted fatally. This case followed diphtheria, and, as was shown at the autopsy, was the result of a staphylococcus infection. Cultures from the heart gave a pure growth of cocci. Holt[27] reports a case from Harris in a child four years of age. The lesion in this instance affected the right side of the heart and was secondary to a cardiac malformation. Another fatal case in a girl fifteen years old is described by Cantley. In this case the pulmonary valve was affected. On the other hand, Adams relates a case of recovery as one of only four hitherto reported under the age of fourteen years.§ The greater proportion of cases reported in early life have been over ten years of age. There are 25 or more of these (Holt), and although the right heart is occasionally affected, the disease, according to Lannois and Paris, seems usually to attack the aortic valves.[28] Loeb describes such a case where there were extensive lesions of this valve, and which followed gonorrhœa. The diplococci found had the morphological appearance of gonococci.

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* Poynton and Paine. Medical and Surgical Society of London, April 8, 1902.

† Year Book, loc. cit.

‡ British Medical Journal, June 13, 1903, p. 1373.

§ Archives of Pediatrics, December, 1902.

While the authoritative cases of ulcerative endocarditis of rheumatic origin are infrequent, such cases are occasionally described. E. Berie[29] reports two such. The bacillus coli is rarely found and seldom exists as a cause. Still, cases are described both by Henchen and by Andrews.

The symptoms of malignant endocarditis vary very much in individual cases. Sometimes the signs pointing to endocarditis are very indistinct, or entirely absent. This is true particularly where the cardiac disease complicates another acute infectious and septic disease like pneumonia, empyema, or meningitis. Herzog, O'Donovan, and others report cases which appear to support this position. Not only is the difficulty of recognition very great by reason of the absence of distinctive signs, but also by the variety of clinical symptoms present. The latency of the disease is sometimes such that a diagnosis cannot be made in the beginning.* Gavala's case is an instance of this sort. In many cases during life there are no cardiac murmurs, and the diagnosis must be based wholly upon the symptoms.† Again, the symptoms may be most misleading and point to a very different disease, as in the two remarkable cases of N. Pitt,[30] in which symptoms at first appeared to be those of spinal disease. The complete absence of fever also in a given case is not an absolute reason for calling in question the diagnosis, as witness the fatal one reported by C. O'Donovan, without fever.[31] In very few cases of Glynn's patients were there rigors, and in some pyrexia was absent for days and weeks at a time. It may be remarked that the former part of this experience is certainly almost unique. The difficulties attending the diagnosis are sometimes insuperable, for trustworthy clinical indications may be wanting. (Glynn.)

In other instances where the malignant endocarditis is subacute or chronic, and complicates an endocarditis of rheumatic origin, it may show distinct signs and is quite easily recognized. In the former cases the autopsy alone reveals the nature of the disease.

Occasionally the differential diagnosis between rheumatic and acute infective endocarditis is practically almost impossible. There is a mild form of malignant, non-septic endocarditis which resembles in many particulars the grave form of septic endocarditis.‡ In this form, while the local symptoms are not dissimilar to those of simple endocarditis, the general condition is notably bad. In this form we have hemorrhages of the skin and mucous membranes, and emboli in various organs, and also joint implications. But though the joints are swollen and tender the inflammatory arthritis remains serous; it does not become purulent. In the graver cases of this type the patient will often succumb after a few weeks' illness to an aggravation of the general condition. On the other hand, the milder cases will often recover.[32] The severe malignant form of endocarditis is almost invariably of septic origin. It is of distinct etiological origin as compared with the milder form referred to. It is characterized apart from cardiac symptoms by the formation of metastatic abscesses in different organs, with or without the accompaniment of hemorrhages. The malignant endocarditis and the metastatic abscesses are directly referable to micrococci; the parenchymatous swelling and changes of organs are the result of the transport of toxins. The microscopic investigation of the different organs often shows the march of the pathological process and how it originated in small foci where minute vessels are filled with micrococci, which later produce areas of cell necrosis, finally leading to suppuration. Because at times no origin at all is discoverable for this form of disease, it seems very obscure. Again, the disease is occasionally not seen by the physician until its later stages, and hence its diagnosis is rendered even more difficult. Very often a pronounced leukocytosis will help us recognize the disease, but the feature of greatest significance is the finding of micrococci in the blood during life. This has already been accomplished more than once. Further bacteriological investigations in this direction are most desirable. Some of these cases run a very chronic course, and one case is reported by Osler where the disease lasted over a year. The autopsy showed extensive vegetations and ulceration of the mitral valve (p. 704). The fever is not always remittent; it may be high and continuous. The rashes, under certain circumstances, may render the disease liable to be confounded with typhoid fever or cerebrospinal meningitis. The sweating is often most profuse. Jaundice is occasionally present and may render confusion with acute yellow atrophy of the liver possible. Cases, even the most acute, usually last a week or more, and yet the disease has been known to terminate fatally in forty-eight hours.

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* Jackson, loc. cit.

† British Medical Journal, May 19, 1900.

‡ Strümpell, p. 307.

Ordinarily, malignant endocarditis is an intercurrent or secondary affection of some primary septic process. The symptoms of this primary state should not therefore be confounded with those belonging to one of its localizations. It is, however, frequently most difficult to differentiate them. Many of the febrile attacks, which occur in cases of chronic endocarditis and which are accompanied with grave symptoms, result in ultimate recovery. It is very difficult in these instances to be sure whether these cases belong to the benign or malignant variety of ulcerative endocarditis during the period of the acute attack. The fact of the recovery, of course, argues strongly in favor of the benign form, although the clinical symptoms closely simulate those of the graver disease.

As to whether an acute endocarditis will be simple or ulcerative may depend somewhat upon the number or nature of the bacteria transported by the blood. Yet as we find the same bacteria in both forms of disease, this position is not wholly tenable. It seems probable that the particular outcome locally, of the fixation of the bacteria, will depend more upon their virulence than any other one factor. It is also true that ulcerative endocarditis is liable to attack those persons suffering from exhausting diseases and the different cachexiæ. In some cases of ulcerative endocarditis the diagnosis is based mainly on the septic symptoms, and there is little or nothing in the local examination of the heart which will throw light on the case. On the other hand, a suddenly developed cardiac murmur, or a distinct and rapid modification of one already existing and showing previous valvular disease, will have great importance in diagnosis. It is necessary, therefore, in all suspicious cases, to make frequent and careful examinations of the heart, and to note all changes of rhythm which occur. The same is also true of the timbre of the murmur which may change at any time, and from being harsh and loud from the previous lesion may become soft and blowing by reason of the fresh disease which has developed. Combined with the heart symptoms are those of sepsis and embolism. The presence of fever and the numerous petechiæ or hemorrhages are always very significant; these symptoms being rarely combined in ordinary rheumatic endocarditis, sometimes the discovery of some evident cause of the septicæmia will bring light to an otherwise obscure case. Thus a foul vaginal discharge, which may be the result of an abortion in which the neck of the uterus has become abraded, will in this way prove satisfactory.

While chills, fever, and sweating point to septic fever, they do not fix the diagnosis of ulcerative endocarditis, and this must be done by examination of, and findings in the heart, or else by the changes due to emboli in the organs. Skin, urine, spleen must be frequently examined with this end in view. When other means fail to establish a diagnosis, an examination of the blood should be made. It is claimed that in most infections there is a decided leukocytosis, but in ulcerative endocarditis this statement is not always correct, according to Neussen, who says there is either an absence or possible decrease of leukocytosis.* On the other hand, Kelly dwells upon the importance in diagnosis of the presence of a moderate leukocytosis of the polynuclear variety. The latter also insists on the positive result of bacterioscopy of the blood. Likewise he attributes much value to the fact of the great instability of heart action, which may be noted in a very brief period. Some cases of ulcerative endocarditis may be readily mistaken for typhoid fever. In the latter, even though of severe type, hemorrhages in the skin are very rare. Moreover, we have earlier enlargement of the spleen, and pronounced abdominal symptoms, usually like tympanites, diarrhœa, distention, and rose spots. In all doubtful cases we should make the Widal test, and sooner or later we expect to get it in typhoid fever. The presence of this test would also help to eliminate acute miliary tuberculosis, with which ulcerative endocarditis might be confounded. Unfortunately, the Widal test is not always absolutely reliable, even when present, to determine the differential diagnosis. One such instance is reported by Mathews and Moir,* where the Widal test was positive, thus confusing the diagnosis with one of typhoid fever. The autopsy showed that the disease was one of ulcerative endocarditis. Some instances, also, are reported, where the Widal test has proved negative. In other cases there has been a positive Widal reaction, and with different strains from one in twenty to one in two hundred. We thus perceive that this reaction is incapable at times of differentiating between these cases.†[33] The serum reaction in the differential diagnosis may be misleading in other instances, notably in septicæmia and acute tuberculosis. (Glynn.) Acute miliary tuberculosis may be differentiated frequently by the presence of tubercle bacilli in the sputum, and also by the preponderance of chest signs over those indicating a heart lesion.‡ I have had one case, unfortunately, of miliary tuberculosis of the lungs under my care, which resulted fatally, in which no tubercle bacilli were ever found, and in which the chest signs were changeable and uncertain for several weeks. In this case there was a soft, blowing murmur at the mitral orifice. There were, however, no hemorrhages of the skin, and no manifest symptoms pointing to emboli in the viscera. At one time there was slight hæmaturia, which made me somewhat suspicious of the renal condition. In a few days this cleared up, and I thought it was explained by renal hyperæmia, due to the febrile nature of the disease. The recurring chilly sensations, profuse sweats, and dyspnœa may occur in both diseases. The loss of flesh and strength may also be marked in both.

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* Babcock. Diseases of the Heart, p. 181.

The temperature chart is probably more irregular and different in ulcerative endocarditis. Here again I have found it very difficult at times to pronounce in which direction I was carried by its careful consideration. As a rule ulcerative endocarditis may be readily distinguished from malaria by the discovery of the plasmodium in the blood, and also by the greater irregularity of the fever and chills which presents the septic type. In what Osler regards as a very remarkable sub-group of this type, the fever and chills may closely simulate regular attacks of quotidian or tertian ague. In those instances where there has been a previously well-marked malarial infection, the differential diagnosis would become additionally difficult. Again, and despite the affirmation of distinguished observers to the contrary, I have met with undoubted cases of malaria, as I believe, in which no malarial organisms have ever been found, and despite careful and repeated microscopic examinations of the blood by skilled observers.

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* British Medical Journal, June 22, 1899.

† Lancet, March 22, 1902.

‡ Thompson. Practical Medicine, second ed., p. 319.

Occasionally chronic endocarditis, accompanied by a fever resembling that of typhoid or remittent fever, may lead to confusion in diagnosis. In these instances, however, embolic phenomena, septic or other, are not found. Moreover, these cases are often prolonged for several months, as in one of Bristow's, cited by Osler. In those cases accompanied with irregular fever, embolic phenomena and physical evidences of recent endocarditis with cardiac distress, and which run an acute course, it is sometimes most difficult to know whether ulcerative endocarditis is present or not. If the case goes rapidly to a fatal termination, as it often does, and we obtain an autopsy, of course the nature of the case can be positively decided. If, on the other hand, the fever, restlessness, cardiac distress, and local signs of heart lesions wholly disappear, and the patient recovers entirely, as in certain recorded instances of gonorrhœal endocarditis (Thayer and Lazear), we may still retain, perhaps, reasonable doubt as to our diagnosis.

The instances which are reported to recover are the less acute forms, and have usually been grafted more than once upon old sclerotic changes of the cardiac valves and orifices. In this category I should be inclined to put some of the gonorrhœal cases. These, however, as we know, are diagnosed at times more by cardiac changes than by septic symptoms.* The mechanical factor in the development of ulcerative endocarditis is not an essential one, inasmuch as the fresh endocarditis does not always arise at the site of the old endocarditis if the latter is present.† The distinction Lenhartz makes between chronic septic endocarditis and malignant rheumatic endocarditis, based on the presence in the former of micro-organisms commonly producing sepsis, is called in question by Litten on the ground of variability of bacteriological conditions, and he states that no distinction can be made on this basis. Stengel finds both classifications unsatisfactory.‡

In these instances much importance should be attached to the supposed etiological factor. If it be of the nature of articular rheumatism, chorea, or scarlatina, we would infer that we had to do with an endocarditis of benign type; if, on the other hand, we find in the antecedents some pus infection or focus of suppuration, puerperal processes, bone-disease, etc., we are prone to believe that ulcerative endocarditis has developed. Again, the febrile movement may be wholly absent, or else pursue a very mild and regular course. In the latter case it is probably due either to the acute endocarditis of simple type, or to the rheumatic cause. When either one gradually subsides the fever also disappears.

With the greatest possible care, however, on the part of the attending physician, the diagnosis of ulcerative endocarditis may be mistaken or overlooked, so frequently do the symptoms vary.§

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* Allbutt, p. 882.

† Lenhartz. Gould's Year Book, 1903, p. 182.

‡ Loc. cit.

§ Thompson, p. 319.

Again, as I have pointed out already, there may be a complete absence of recognizable cardiac signs locally. In the acute classes resembling cerebrospinal fever, blood cultures do not help us very much to make an accurate differential diagnosis. If the spinal disease be of tuberculous nature, puncture of the spinal membranes and withdrawal of fluid may be of very great value in revealing the presence of tubercle bacilli. In the non-tuberculous variety, whether it has become suppurative or not, we may find the same organism that is discovered in ulcerative endocarditis, and of course our doubts are in that case not solved by this method of exploration.

The course of ulcerative endocarditis may be very brief. Indeed, it may be a very acute disease, last only a few days, and then terminate fatally. Such are the extreme and relatively rare instances. The more frequent ones are those where the disease has lasted several weeks. Its progress onward and downward may be continuous. On the other hand there may be periods of relative improvement followed by renewed exacerbations. The patients seem to improve for a time and subsequently relapse and return to the hospital in a worse condition. (Glynn.) When death actually occurs it is occasioned by the progress of the heart disease, which finally causes pronounced asthenia. Or again it is the prolonged general sepsis which apparently occasions the fatal outcome. There may be complicating pulmonary œdema or pneumonia, and in this way death occurs more rapidly. Sometimes it would appear that the term of life is closed essentially by reason of emboli in different organs—kidney, spleen, or brain.

An interesting case is reported by Babcock (p. 173 *et seq.*) following an attack of tonsillitis which after five months' duration terminated fatally. In this case, although clearly a septic one from the beginning, the pulse persisted at about the same rate (105), and there was a fairly continuous temperature with slight changes. There was present marked bulbous enlargement of the terminal phalanges of the fingers due to capillary dilatation. Unfortunately in Babcock's case there was no autopsy. Credé's ointment and antistreptococcic serum were employed, with the results perhaps of increasing strength for a while, and occasioning a slight reduction of temperature. The occurrence of emboli always renders the prognosis more serious. In addition to the mere mechanical results of these emboli in the different viscera we observe their septic consequences, which contribute to the speedy, fatal termination. Thus we find single or multiple septic abscesses in the spleen, liver, kidneys, and, indeed, throughout the body, and these are the evidences of general infection of the economy. Of course, death is the inevitable result, almost, of such a condition.

In general the treatment of ulcerative endocarditis is that of acute benign endocarditis with even greater precautions exercised about preserving the strength of the heart, noting that independently of the specially destructive tendencies of the disease to the cardiac valves and walls and the formation of abscesses locally in its structure the heart muscle is more likely to suffer from the effects of the toxæmia itself than in the relatively benign form of disease. The treatment may be regarded therefore as essentially symptomatic.

To combat general sepsis we should rely upon large and repeated doses of alcohol in the most palatable and useful form—*i. e.*, the best old brandy—alternating it with best champagne now and then for a day or two. The employment of alcohol in septic disease and in sufficient quantity is still heartily endorsed by many eminent clinicians and despite many and strong arguments made use of by its adversaries. Carbonate of ammonia is also possibly a useful adjunct to alcohol for a little while, in view of the thrombotic findings upon the cardiac valves which some autopsies reveal and by reason of the proofs we seem to have, clinically, of its action in lessening somewhat the tendency to such deposits or formations. The late Dr. Benjamin Ward Richardson insists forcibly upon this view as regards certain infectious diseases, notably diphtheria, and I have always believed with much reason. I am satisfied, however, that carbonate of ammonia is far more depressing even than alcohol if too long continued, and particularly in large, frequently repeated doses such as are so often insisted upon in clinical text-books of practice of medicine.

To abate or lessen the chills and the fever quinine is used by some with the idea that it will do so if given in doses of 5 to 10 grains three or more times daily. With our improved knowledge of the etiology and pathology of the disease such a view seems scarcely warranted. And when we think of the cardiac depression which may follow such doses, demonstrated many years ago by Binz, I find no adequate reasons for the use of the drug after this manner. The treatment of disease then, according to many, is practically that of septicæmia (Osler), and except the measures which we should rationally employ in all forms of endocarditis even the mildest.

Are there therefore no known measures which have any curative influence upon the march and termination of the disease itself? Dreschfeld speaks of having been useful by means of a combination of quinine and arsenic in 3 cases, 2 of which he reports.[34] In neither case, however, did recovery take place. Perhaps the prognosis of ulcerative endocarditis may become more hopeful with our improved forms of treatment; more so even than that of the cases of endocarditis which are regarded as relatively and less immediately dangerous.

With the progress of serotherapy and of intravenous medication this statement has become especially true during the past year. This progress is due to researches of pathologists who, like Poynton and Paine, have pointed out the parasitic nature of the disease.

Besides, several histories have been reported pointing to the favorable outcome of the disease through medication. Occasionally recovery may be expected. Clinical reports bear evidence of this, and besides it is more than justified by the results from autopsies.

The treatment of the disease has now definitely in view the killing of the germs. Two methods of medication have been tried —*i. e.*, the sera and the mineral germicides. They may be administered either internally by mouth or rectum, subcutaneously or intravenously. Later all three methods may be combined at the same time to hasten the cure.

As to the relative value of these remedies it is impossible to state at present. But each day seems to show how important has become the interactions between living and inorganic matter. In this line notably are the effects of radium on the tissues. The promulgation of the catalytic action of sera and albuminized metals is also related to our ignorance, but presuming this theory to be correct it would prove how useful the direct application of remedies may be to the cure of disease. An effort has been made to introduce antiseptic remedies in sufficient quantity into the system to exert at least a modifying influence upon the sepsis. (Babcock.) Among these the sulphocarbolate of soda in one-half drachm doses has been used by Sansom, and with such good effect that one patient was enabled to leave the hospital and remain away ten months before a fresh attack occurred. To the latter, however, she succumbed, and the autopsy justified the accuracy of the diagnosis by revealing cardiac valves permeated with micrococci.

Of course if antiseptic medication is to be of real service it must be employed in sufficient amount to affect the system thoroughly, and be continued for a considerable period. And here resides the danger with which we are all familiar, to-day more than ever, that in our efforts to destroy or neutralize micro-organisms and their toxins so pernicious to the economy, we may occasion great harm to the composition of the blood which would more than counterbalance any beneficial results from the use of antiseptic medication. This is especially true if we employ the hypodermic method. In illustration I would refer to the brilliant work of Barrows in the treatment of puerperal septicæmia, who at first seemed to have achieved a very remarkable triumph.

According to the latest laboratory experiments of J. M. Fortescue Brickdale,[35] injection of antiseptics produce no favorable results. This experience is corroborated by W. H. Park and W. A. Payne,[36] who state that in their judgment the use of plain salt and water intravenously will be found equally useful and less dangerous than diluted formalin injections.

On the other hand the use, clinically, of intravenous injections of antiseptics by Netter,[37] Maguire, Landerer, and Ewart, has been at times distinctly favorable. Further, Klotz narrates a case resulting successfully, in which colloidal silver was used hypodermically. After two injections there were rigors and no improvement; but after the third there was rapid decrease of fever and ultimate recovery.[38]

As Ewart remarks, forcibly, too rigid adherence should not be directed toward mere "germicidal potency" as a test for practical utility. It may be that intravascular antisepsis will prove delusory, but over and beyond is the great subject of intravenous medication which must remain as a very valuable aid to our methods of treatment. Inasmuch as the action of the antiseptic injections is not bactericidal, some other explanation must be given of their power for good. According to Netter this resides in a catalytic action much resembling the action of ferments, and depends upon a mysterious power of matter. In the discussion of Dr. Barrows' paper the majority seem to preserve an open mind as to the desirability of the treatment in any extensive way.[39]

O'Brien[40] has pointed out some of the dangers resulting from intravenous injections—*i. e.*, rigors, collapse, and respiratory embarrassment. In one case sudden death followed. As there was no autopsy a definite explanation could not be given. It is important to note that those who make use of these injections should be prepared to deal with sudden emergencies which may arise.

No doubt there is some comfort to be taken, as Babcock would have us believe, apparently, from the neutralization of the toxins found in the intestinal tract during the course of ulcerative endocarditis, and which doubtless, unless properly neutralized, tend to aggravate the original disease and prevent recovery. Among these so-called antiseptics used to modify favorably autointoxications from the intestinal tract, there are only a few in which I have at present even limited confidence. The best and least harmful which I have tried are small, repeated doses of beechwood creosote, the salts of bismuth, and wood charcoal. In a paper read before the New York Clinical Society about two years ago I directed attention in this connection to these drugs, and spoke favorably of their use as compared to others I had tried.

Up to the time of writing a certain number of cases have been treated by the antistreptococcic serum, and with more or less success. There is a certain degree of reason in the use of this serum, because it appears to be useful in other septic cases—notably puerperal septicæmia. It is also reasonable to employ it because streptococci are undoubtedly among the organisms which appear frequently infiltrated, as it were, in the cardiac valves at the autopsy of these cases. The serum itself, properly employed, does not cause injury to the patient, and again we find in the antitoxin treatment of diphtheria an analogy which makes us somewhat hopeful of this other new treatment. The outlook seems to be, therefore, that pathological sera will probably be more and more used. Antitoxins and immunizing sera have, indeed, more than one action, and, it has been demonstrated, may be useful in distinct diseases. The explanation of their effects may reside in a catalytic action not dissimilar to that of the albuminates of the metals. The intravenous route is the one now preferable for serotherapy, especially in the severer cases, and when subcutaneous injections have proved ineffective. To the former injections, despite disadvantages and dangers, we should recur hopefully.

Sir Douglas Powell reports three successful cases from the use of antistreptococcic serum, and emphasizes the fact that if it were employed earlier in the disease, and before a general dissemination of it in different organs had taken place, our results would be better. He also considers that in its use we must not expect benefit where organisms of another order, like pneumococci or gonococci, are present, but be hopeful and limit its use to those cases in which streptococci or staphylococci have been causative. If there be anywhere a purulent focus which surgery can reach it must be promptly dealt with and suppressed if possible. Otherwise we should expect continual accessions from this source of the toxic organisms whose influence we wish to combat. Hence, the employment of the antistreptococcic serum must remain useless. On the other hand, if the supply of toxic-bearing bacteria is stopped, and even though many of those already in the blood may be other than streptococci, this serum may prove very beneficial.

To obtain our best, most hopeful results treatment should be begun at an early date, or so soon as the diagnosis approaches a high degree of probability. There are, moreover, evident grades in the malignancy of different cases of ulcerative endocarditis, and it is impossible at first to pronounce as to the precise future course of a given case of the disease. The reported cases of improvement and recovery under more than one sort of treatment makes this fact very clear. Again, we should be encouraged from this standpoint to begin early treatment with the serum. It is always judicious and advisable also, to take blood in a doubtful case for the purpose of culture inoculation and other experiment, even though no profitable determination can always be made so as to fix, if possible, the cause of the disease. (Gibson, quoted by Babcock.) Great care must be taken that the blood obtained for bacteriological examination should not be contaminated. The staphylococcus albus, if found, is due to contamination, and is not the specific cause of the disease. The micro-organism which is most frequently found by cultivating the blood is the micrococcus pyogenes. It has been obtained in many cases of ulcerative endocarditis. If a patient with some valvular disease has irregular temperature, is anæmic, and streptococci are obtained from cultivation of the blood, a diagnosis of ulcerative endocarditis should be made, and the indication is to inject antistreptococcic serum. Blood examination should not be considered infallible as an aid to diagnosis and prognosis. As Bryant[41] writes in corroboration of Ewing's statement: "The examination having been performed, its results are to be interpreted only in the light of the fullest possible clinical information."

It would appear that ulcerative endocarditis of pneumococcic origin offers little hope for any beneficial result from this treatment. Let us hope that the day is not far distant when a suitable serum will be available for every kind of septic poisoning, no matter what the precise efficient bacterial cause may be. The modern researches of the Klemperer brothers and others give us renewed trust that our wishes may soon be realized. (Babcock.) From 3 cases reported by Babcock he is evidently disposed to make use of the antistreptococcic serum in any future cases he may see, even though the diagnosis may be somewhat doubtful, and provided other treatment has been used in vain. He remarks with justifiable emphasis: "Such cases are so desperate and the prospect of recovery so slight that I believe one is justified in resorting to whatever affords even a chance of benefit; and if an old preparation is employed there is not much danger of producing erythema or articular inflammation, and the remedy cannot prove more harmful than the disease itself, unchecked."* Successful results in the use of antistreptococcic serum in the treatment of ulcerative endocarditis have been reported by Sainsbury and by Pearce,[42] another also by Clarke.[43] The following case reported by Bryant[44] appears to me very convincing: "A boy, aged fifteen years, was admitted to the hospital suffering from mitral disease. He had had several attacks of rheumatism. His temperature was varied and running an irregular course, ranging between 98° and 101.5° F. When he first came under my care he had been in the hospital for nearly two months, and during the whole of the time his temperature had been raised and he had not had any manifestations of rheumatism or of tonsillitis. A bacteriological examination of the blood showed the presence of streptococci in pure culture. A few days afterward the temperature dropped to normal and remained normal. A subsequent bacteriological examination of the blood was negative. I considered this boy was suffering from infective endocarditis, that the acute process had subsided, and the streptococci died out."

In some cases of ulcerative endocarditis treated with antistreptococcic serum, while temporary benefit may result from its use, the result ultimately has been fatal. An instance of this kind is described by H. M. Cooper.† In this, as in other cases, it was thought if the serum treatment had been instituted earlier a succesful result might have been obtained. Per contra, as regards the matter of the innocuousness of these injections, the following cases are interesting and important. B. M. H. Rogers[45] used five injections of 10 c.c. each of antistreptococcic serum in a case of ulcerative endocarditis, in which pure cultures of streptococcus had been obtained from the blood. The injections caused violent pain, were without effect, and death occurred. Post-mortem cultures yielded streptococci. J. H. Abram[46] reports another case treated in a similar manner after streptococci had also been found in the blood. The case was fatal; but it was found after death that the streptococci had disappeared. The serum is believed to have caused this disappearance.

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* Loc. cit., p. 797.

† British Medical Journal, May 10, 1902.

Cyril Ogle[47] indicates the value of antistreptococcic serum in cases in which the symptoms during life, or the post-mortem findings, showed ulcerative endocarditis. Of course, the cases are not favorable ones in view of the constant passage of the blood current over the surface of the affected organ—*i. e.*, the heart. Still, recovery is not incompatible with this grave infection when thus treated. In Dr. Ogle's table the successes amount to 31.5 per cent.; in Sir Douglas Powell's tables, to 25 per cent.[48] On the other hand, Nathan Raw used antistreptococcic serum in 5 cases without any beneficial results. And Glynn reports no information of an encouraging nature from Liverpool hospitals, and without success in 3 of his own cases. I find 1 successful case reported by Moritz,[49] in which antistaphylococcic serum was employed. Six injections of 5 c.c. were sufficient to dissipate the acute symptoms. When they were begun the patient had been ill during two months. In two weeks of treatment the temperature was normal. Six weeks later a heart murmur was present and the pulse was rapid. Still the man remained in good condition.[50] Other methods of treatment have also been followed by reported cures. One by Coleman which followed vaccination. Another from Hepburn in which the treatment was entirely symptomatic. In one instance the aortic murmur disappeared during convalescence. The treatment was by the Brand method and unguentum Credé.[51] Roussell[52] reports three recoveries. Another recovery of gonorrhœal endocarditis is from a paper of Lenhartz.*

The employment of yeast in the treatment of ulcerative endocarditis is referred to by Sir Douglas Powell, and 1 successful case out of 5 is reported by him. In the other case there was no appreciably good result. In one other instance where nuclein was employed there was a decided lowering of temperature. The remedy was employed subcutaneously. If yeast has any remedial value it is probably due to the nuclein or nucleinic acid it contains, as instanced by Vaughn. The latter may be used by mouth, rectum, or hypodermically, according to the strength and kind of preparation made use of. It would seem as though the curative action of the nuclein was essentially due to its power of increasing polynuclear white cells. These, as we know, are frequently more numerous in ulcerative endocarditis, and the germicidal properties of nuclein are explained by their additionally increased number. Many favorable reports, according to Babcock, have been made about the value of yeast-nuclein in the treatment of divers pus infections. And in view of these statements he was encouraged to give it a trial in a case of acute endocarditis complicating a follicular tonsillitis, possibly of rheumatic origin. During the period the remedy was taken the fever slowly abated. Despite this fact, however, the case terminated fatally. Latterly, Duckworth reports, in the Section of Medicine of the Fourteenth International Medical Congress (Madrid, April 25, 1903), a case of probable ulcerative endocarditis in which a treatment with fresh yeast and antistreptococcic serum hypodermically was employed without appreciable benefit. Subsequently, however, a cure was apparently effected by repeated injections per rectum of a mixed antistreptococcic serum, 10 c.c. being the dose employed.* "This case may be taken," writes Duckworth, "to illustrate the effects of a specially virulent quality or variety of the specific infecting microbe which commonly induces ordinary rheumatic symptoms, and may add support to the view of Poynton and Paine that infective endocarditis may sometimes be a primary affection due to a virulent form of the peccant matter of rheumatism."

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* Loc. cit.

If all endocarditis should be properly regarded as infective, it is indicated to find our remedial agent among the class of antiseptic remedies. The most available and least objectionable is the one to make trial of. Amidst the rapidly increasing number of this class of remedies one will be ultimately found that is decidedly curative in many instances. Of course, in making use of the antiseptic remedy so as to influence the entire mass of blood and prevent the infection from being carried to and localized upon the endocardium, we should avoid strictly employing remedies which threaten the general health. At present, moreover, we make use of such remedies mainly in the treatment of the supposed virulent cases, and usually at a later stage of the disease when the outcome is almost surely fatal. In the far larger class of benign cases of endocarditis, and hence the more important ones, their progress is often not stayed by this or any other careful treatment soon enough. The result is they continue their onward insidious and disastrous march. If these cases were treated in the beginning by judiciously selected antiseptic remedies, it is to be hoped that eventually we should have fewer cases of both sorts, and mainly, I believe with Ewart,[53] of the ulcerative forms. Further, we should not be obliged to admit, as it seems to me, with the writer of the latest and most valuable treatise on diseases of the heart, "that the most the physician can do in the treatment of acute endocarditis is to aid nature by helping to maintain the vital powers that lie in nature's way."[54] Let us remember that recovery in an apparently desperate case is possible, and the future may bring improved methods both of serum and antiseptic treatment.

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* Lancet, May 2, 1903, pp. 1268, 1269; and Boston Medical and Surgical Journal, August 29, 1903, p. 238.

† British Medical Journal, May 23, 1903, p. 1195.

It may be well to add that the latest experiments upon animals seems to prove that the Aronson antistreptococcic serum is superior to the others, notably those of Marmorek and of Tavel. It is apparent, also, that to obtain the best curative effects the serum should be given intravenously. Also, treatment according to this method should be continued well into the period of convalescence, inasmuch as death occurs sometimes when all danger seems to have passed.

Finally, I would again insist upon the primary importance in all cases of beginning the use of the serum at an earlier date than hitherto has usually been done. Sometimes, not to say frequently, it has been employed when all curative methods must prove futile, as the economy is unable to respond favorably to that as to all other medication. Moreover, whenever the infection has lasted more than a very brief period much larger doses of serum are rendered necessary to produce similar curative effects. I shall not attempt to explain how the serum acts. Nor, indeed, is it positively known. Certainly it has no appreciable effect upon the growth of cocci in the culture tube, and it appears in final analysis merely, so far as our knowledge now extends, to diminish *virulence*, "for cocci which have been left for some time under the influence of the serum will no longer bring about hæmolysis."[55] The latest paper on the use of "antistreptococcic serum in the treatment of inflammatory rheumatism and other diseases" is to my mind very encouraging. It shows conclusively it is most efficient when given *early* in infectious disease; also, that it is useful in *diplococcic* infection. In Dr. G. H. Sherman's[56] cases "none of the patients developed heart complications, and complete recovery took place in a comparatively short time." This statement contradicts that of Osler—*i. e.*, "We know no measures by which in rheumatism the onset of endocarditis can be prevented."[*]

BIBLIOGRAPHY.

1. Medical News, March 21, 1885.
2. London Lancet, March 25, and April 2 and 9, 1898.
3. Loc. cit., April, 1903, p. 1153.
4. Practice of Medicine, 4th ed., p. 699.
5. Loc. cit., p. 700.
6. Progressive Medicine, September 1903, p. 79.
7. Practice of Medicine, 6th ed., p. 595.
8. C. S. Bull. Medical Record, December 20, 1902.
9. Johns Hopkins Hospital Bulletin, October, 1902.
10. Progressive Medicine; also Deut. med Woch., May 22 and 29, 1902.

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[*] Vide fifth edition, 1903, p. 705.

11. To show the extreme rarity, even with typhoid fever, I would cite Dr. Osler's medical clinic at the Johns Hopkins Hospital, where there never has been a case (written communication from Dr. W. S. Thayer, December 10, 1903). Very probable cases, in view of the symptoms during life, are occasionally met with. Even in fatal cases with characteristic symptoms, where no autopsy is obtained, doubt as to diagnosis may be urged, although in one of Dr. Thayer's cases such doubt would hardly be justified.

12. Wells says this complication is very frequent.

13. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1901, p. 53.

14. Austen. Johns Hopkins Bulletin, 1899, p. 104.

15. American Medicine, October 17, 1903, p. 627.

16. Journal of Experimental Medicine, 1899, p. 521.

17. Journal of the American Medical Association, August 19, 1900.

18. Progressive Medicine, September, 1903.

19. Gould. American Year Book of Medicine and Surgery, 1903, p. 752.

20. Progressive Medicine, September, 1902, p. 128.

21. Allbutt's System of Medicine, vol. vi. p. 876.

22. Practice of Medicine, 4th ed., p. 701.

23. The vegetations themselves, although unrecognized during life, may have been present for a long while, as shown by autopsy.

24. Dessy. Boston Medical and Surgical Journal, September 1, 1898.

25. Journal of Experimental Medicine, January, 1899.

26. Rev. mens. des mal. de l'enfance, December, 1898.

27. Diseases of Infancy and Childhood, 2d ed. p. 622.

28. The exceptions to this rule would appear to be cases of gonorrhœal origin where the right heart is frequently involved (Thayer and Lazear).

29. Semaine méd., January 21, 1900.

30. Practitioner, November, 1898.

31. Medical News, July 23, 1898.

32. The duration in the fatal cases is only a few days or weeks, but in those that recover it is usually much more prolonged.

33. According to MacFarland there was in 4000 cases only 4 per cent. of error (Babcock, p. 182). If after sixth day of illness test is negative, typhoid fever may be properly excluded (Allbutt, foot-note).

34. Allbutt's System of Medicine, vol. vi. p. 884.

35. Lancet, January 10, 1903.

36. Medical News, April 4, 1903.

37. Bull. et mém. de la Soc. des hôp. de Paris, December 18, 1902, et seq.

38. Progressive Medicine, September, 1903, p. 81.

39. New York Medical Journal, January 31, 1903.

40. Lancet, October 11, 1902.

41. Ibid., February 7, 1903, p. 364.

42. Allbutt's System of Medicine. Loc. cit., p. 885.

43. Lancet, July 21, 1900.

44. Ibid., February 7, 1903, p. 364.

45. Ibid., June 10, 1899.

46. Ibid., February 25, 1899.

47. Ibid., March 14, 1903.

48. Ibid., April 25, 1903, p. 1153.

49. Serum therapie bei Endocarditis Maligna, St. Petersburger medicinische Wochenschrift, 1898.

50. In Moritz's case the diagnosis of the organism present had not been confirmed previously by a blood examination, although the evidence of implication of the valves seems to have been certain (Lancet, March 14, 1903, p. 723).

51. Philadelphia Medical Journal, January 12, 1901.

52. Ibid., February 23, 1901.

53. Progressive Medicine, September, 1902, p. 112.

54. Babcock, p. 198.

55. Medical News, September 5, 1903, p. 462.

56. American Medicine, October 17, 1903, p. 633.

NOTE.—Owing to the length of this paper, I am obliged to omit the histories of my cases.

In Bulletin of the Ayer Clinical Laboratory of the Pennsylvania Hospital, October, 1903, a unique case is reported of ulcerative endocarditis caused by Weichselbaum's meningococcus.